

REMARKS

Favorable reconsideration of this application is requested in view of the following remarks.

The specification has been amended to clarify which primer corresponds to which sequence identifier of the two.

Figs. 1A, 3B, 4A, 4B, 6B, 8B, 9A, 9B, 9C, 10A, 11A, and 11B have been amended by adding the sequence identifiers SEQ ID NOS: 23-57 to the corresponding peptides appearing in these figures. Accordingly, the sequence listing has been amended to include the sequence identifiers SEQ ID NOS 23-57 as discussed below.

Non-elected claims 6-18 have been withdrawn with traverse.

Claims 19-21 have been added as supported by the specification at page 5, lines 7-11, page 6, lines 11-13, and Fig. 4B, respectively.

Claim 1 has been amended following the Examiner's suggestion to clarify that the polypeptide may be isolated from a natural origin or synthesized as supported by the specification at page 5, lines 19-21 and examples 2-3 appearing at page 11, line 9 – page 12, line 29. Claim 1 has been amended further to include limitations of original claims 4 and 5 and limitations supported by Figs. 4B and 7 and the specification at page 5, lines 1-6 and page 6, lines 13-34. Accordingly, claims 4 and 5 have been canceled without prejudice.

Withdrawn claims 6 and 7 have been amended to include the term “isolated or synthesized” to coincide with claim 1. Withdrawn claim 7 has been amended further to include the limitations of the fragment of the Notch protein in claim 1. Withdrawn claims 13, 15, and 17 have been amended editorially.

The polypeptide sequences disclosed in Figs. 4A-4B and 6B and the primer sequences in the specification at page 7 were considered not to comply with 37 CFR 1.825. Figs. 1A, 3B, 4A, 4B, 6B, 8B, 9A, 9B, 9C, 10A, 11A, and 11B and the specification have been amended in accordance with 37 CFR 1.821-1.825, including the corresponding sequence identifiers. The substitute sequence listing that includes SEQ ID NOS: 23-57 in a computer readable form is attached hereto. Further, Applicants hereby state that the amendments made and included in the substitute sheets of the sequence listing are supported in the application, as filed, at the original sequence listing, original Figs. 1A, 3B, 4A, 4B, 6B, 8B, 9A, 9B, 9C, 10A, 11A, and 11B, and the specification and do not include new matter.

Claims 1, 4, and 5 have been objected to because of informalities. Claims 4 and 5 have been canceled. Claim 1 has been amended to exclude a term “novel” and include “a nucleus of the cell” instead of “a nucleus”. In addition, claim 1 includes “Site-2 cleavage site”, “Site-3 cleavage site”, and “Site-4 cleavage site” with their locations instead of “S3” and “S4”. Accordingly, this rejection should be withdrawn.

Claims 1-5 have been rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Applicants respectfully traverse this rejection.

Claim 1 specifies that the polypeptide is isolated or synthesized. Therefore, this rejection should be withdrawn.

Claims 1-5 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection.

Claims 4 and 5 have been canceled, and the limitations of these claims are included in claim 1. In claim 1, the polypeptide is defined as a fragment of Notch protein that is produced and released as a result of a series of proteolysis. Claim 1 recites sufficient details of the proteolysis so as to be understood readily. Accordingly, this rejection should be withdrawn.

Claims 1-5 have been rejected under 35 U.S.C. 112, first paragraph, as not complying with the written description requirement. Applicants respectfully traverse this rejection.

Claims 4 and 5 have been canceled, and the limitations of these claims are included in claim 1. Claim 1 requires that the Notch protein is the same protein as that existing in a human, a mouse, a rat, a rabbit, a goat, a swine, a bovine, a drosophila, or a nematode. Among these species, presence of F-N β s, i.e., the polypeptide of claim 1, from mouse Notch protein is confirmed by electrophoresis (see for example, Figs. 1B and 1C, and experiment 1 at page 10, lines 24-28 and page 10, line 32 – page 11, line 4). The electrophoresis is a well-known method in the art to separate peptides, RNAs, or DNAs and obtain a particular peptide, RNA, or DNA. In addition, in experiment 3, molecular weight of N β was measured (see a peak at 3832 in Fig. 3A and page 11, line 27 – page 12, line 11). The bands of F-N β s in the electrophoretograms and the mass spectrum in Figs. 1B and 1C, and Fig. 3A, respectively, and methods to prepare samples such as the Pulse-chase method (see page 8, line 27 – page 9, line 2), the method of Immunoprecipitation/SDS-PAGE (see page 9, lines 4-20), and the method of Immunoprecipitation/MALDI-TOF MS analysis (see page 9, lines 21-37 and page 12, lines 2-5) sufficiently show that the polypeptide was isolated by these methods and was in possession of Applicants at the date of filing. Accordingly, this rejection should be withdrawn.

Claims 1-5 have been rejected under 35 U.S.C. 102(b) as being anticipated by Mumm et al. (Mol Cell 5: 197-206, 2000). Applicants respectfully traverse this rejection.

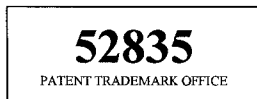
Claims 4 and 5 have been canceled, and the limitations of these claims are included in claim 1. Mumm discloses the Site-2 cleavage and the Site-3 cleavage, which are NEXT producing cleavage (see page 199, coln. 1, lines 6-8), and suggests a cascade model in which NEXT is produced at the cell surface and subsequently converted to NICD (see page 200, coln. 2, first para. lines 14-18 and page 201, coln. 1, lines 7-9). The reference, however, fails to disclose the Site-4 cleavage site of the Notch fragment, which

may be C-terminal of the fragment of the Notch protein, i.e., the polypeptide of claim 1, and may be positioned on a N-terminal side of the Notch protein relative to the Site-3 cleavage site. Accordingly, claim 1 is distinguished from Mumm, and this rejection should be withdrawn.

Claims 1-5 have been rejected under 35 U.S.C. 102(a) as being anticipated by Okochi et al. (EMBO J. 271(20): 5408-54196, October 2002). Applicants respectfully traverse this rejection.

The verified translation of priority document JP 2002-210040 of the present application on July 18, 2002 was submitted on June 18, 2008. The Okochi reference could not be published before August 21, 2002, which is a date of acceptance of this paper (see last two lines at page 5416 of Okochi). Accordingly, the Okochi reference cannot be 35 U.S.C. 102(a) prior art against the present application, and this rejection should be withdrawn.

In view of the above, Applicants request reconsideration of the application in the form of a Notice of Allowance.

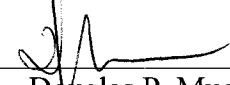


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DPM/my/ad

Respectfully submitted,

HAMRE, SCHUMANN, MUELLER &
LARSON, P.C.
P.O. Box 2902
Minneapolis, MN 55402-0902
(612) 453-3800

By: 
Douglas P. Mueller
Reg. No. 30,300